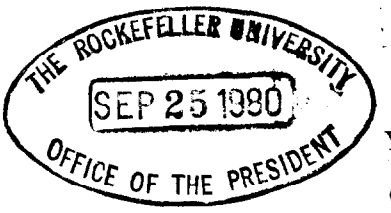
The Population Council

Center for
Biomedical Research



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September 25, 1980

Dr. Joshua Lederberg
President
The Rockefeller University

Dear President Lederberg:

I regret very much that I did not come to see you in January after you invited me to do so at your Christmas party. You may recall that I was the student that provided you with Lactobacillus bulgaricus Sarles, a strange bug that requires lactose and led us to the discovery of pantetheine. We had quite a laugh because you remembered the bug well but you didn't remember me.

But now that my year here at the Population Council is coming to an end, I feel a talk could be much more fruitful. This has certainly been one of the most interesting research years in my career due in no small measure to the cooperation and encouragement of Dr. Bardin. I am sure you understand that it is with considerable regret that I return to the University of Georgia. I have recently learned of your interest in establishing a large effort in Reproductive Biology at Rockefeller University. I am exploring the possibility of spending the next few years in the New York area on a part-time, consulting, advisory or on some other basis.

Let me encapsulate briefly what I and members of the Reproduction Research Laboratories at Georgia have accomplished in recent years. Upon switching to the reproduction field in 1960 it became apparent that virtually nothing was known about the molecular events of how the mammalian sperm enters the egg. In 1967 we initiated an effort in this area and in a few months we demonstrated the existence of a corona radiata penetrating enzyme and have now demonstrated that the sperm possesses an array of esterases to enable it to traverse this cellular layer. We then found a proteinase that was very high in the sperm acrosome and established that sperm use this enzyme to digest a passage through the zona pellucida. We isolated, characterized and determined the specificity of this enzyme and named it acrosin. We discovered acrolysin which converts proacrosin to acrosin and have indications of the presence of at least two additional proteinases and an amino peptidase that very likely serve as back-up enzymes to facilitate the passage of the sperm through the zona. There are several additional enzymes present in the acrosome, glycosidases and ATPases, the nature and function of which we are investigating.

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We are at present also studying the proteins and co-factors that contribute to the acrosome reaction, an event essential for fertilization. Of equal or perhaps greater importance is our effort to isolate, demonstrate and characterize the approximately ten natural anti-fertility substances that exist in mammalian seminal plasma. Discovery of these natural inhibitors led to exploration of synthetic enzyme inhibitors of acrosomal enzymes as anti-fertility agents. This was a wholly new contraceptive approach and it now appears that we have innocuous and effective substances which may ultimately be of medical value.

Finally, I am gratified that so many young scientists who trained in my laboratory at the University of Georgia, under conditions that were less than optimal, have gone on to become some of the most productive and creative in the field of Reproductive Biology.

I am due to leave on October 9th and hope we can get together before then. I have asked Tom Jukes to write to you and I will be glad to provide further references. My C.V. is enclosed.

I am looking forward to hearing from you.

Sincerely,

William L. Williams

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Director
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